

AD _____

Award Number: W81XWH-11-2-0231

TITLE: Plasticity-Based Adaptive Cognitive Remediation (PACR) for OIF/OEF Veterans: A Randomized Controlled Trial

PRINCIPAL INVESTIGATOR: Henry W. Mahncke, Ph.D.

CONTRACTING ORGANIZATION: Brain Plasticity, Inc., San Francisco, CA 94105

REPORT DATE: October 2012

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE			Form Approved OMB No. 0704-0188		
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.					
1. REPORT DATE October 2012		2. REPORT TYPE: Annual		3. DATES COVERED 30September2011-29September2012	
4. TITLE AND SUBTITLE Plasticity-Based Adaptive Cognitive Remediation (PACR) for OIF/OEF Veterans: A Randomized Controlled Trial		5a. CONTRACT NUMBER			
		5b. GRANT NUMBER W81XWH-11-2-0231			
		5c. PROGRAM ELEMENT NUMBER			
6. AUTHOR(S) Henry W. Mahncke E-Mail: henry.mahncke@brainplasticity.com		5d. PROJECT NUMBER			
		5e. TASK NUMBER			
		5f. WORK UNIT NUMBER			
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Brain Plasticity Inc., San Francisco, CA 94105		8. PERFORMING ORGANIZATION REPORT NUMBER			
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012		10. SPONSOR/MONITOR'S ACRONYM(S)			
		11. SPONSOR/MONITOR'S REPORT NUMBER(S)			
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT Our work over year 1 of this project has exclusively focused on the contractual and regulatory issues required to launch a multi-site trial with VA and military hospital sites funded through the CDMRP process, and in the preparation of the training and data collection materials required to execute the study. As expected, this process has been time-consuming; however it is nearly complete (see below) and we anticipate enrolling the first study participant in Q1 2013.					
15. SUBJECT TERMS traumatic brain injury, tbi, concussion, persistent post-concussive symptoms, cognition, cognitive function, cognitive rehabilitation, cognitive training, clinical trial					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON USAMRMC
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U			19b. TELEPHONE NUMBER (include area code)

Introduction:

Traumatic brain injury (TBI) has been described as “the signature injury” of the war in Iraq and Afghanistan. The long-term impacts of chronic cognitive symptoms following TBI for active military personnel, veterans, their families, and for American society as a whole is only now beginning to be appreciated. We have developed a novel treatment program that can deliver effective brain-plasticity-based cognitive remediation (“PACR”) to veterans and active duty military personnel suffering from persistent post-concussive symptoms (PPCS) following mild traumatic brain injury (mTBI) at any internet-connected computer, under the controlled, monitored, quality-assured remote guidance of trained clinical providers. PACR holds tremendous promise because 1) the *innovative therapeutic approach* differs from current treatments in that it uses the principles of brain plasticity to restore, insofar as is possible, the brain’s capacity to process information with high accuracy and efficiency, 2) it implements a *practical and novel delivery approach* with a web-based implementation that can assure the provision of essential cognitive remediation to active personnel and veterans in need of help wherever they may be, and 3) a *significant body of randomized controlled clinical trial data* demonstrates that PACR improves cognitive and real-world function in people with the mild cognitive impairment typical of PPCS following mTBI. Given the substantial unmet medical need in these patients, the basic science rationale and the demonstrated clinical evidence for a brain-plasticity-based cognitive remediation approach, and the scalable technical solution, we propose a clinical trial of PACR in people with PPCS following mTBI. The final product of the activities funded from this grant will be the establishment of a complete brain-plasticity-based cognitive remediation system for use by the Veterans Affairs (VA) and the military that provides scientifically validated, clinically supervised treatment with demonstrable outcomes, delivered in a highly cost-effective and readily scalable form.

Body: Our work over year 1 of this project has exclusively focused on the contractual and regulatory issues required to launch a multi-site trial with VA and military hospital sites funded through the CDMRP process, and in the preparation of the training and data collection materials required to execute the study. As expected, this process has been time-consuming; however it is nearly complete (see below) and we anticipate enrolling the first study participant in Q1 2013. Below is a list of research-related activities, organized by the key activities in our approved statement of work.

1. **Task 1:** Update protocol if necessary. We worked with the principal investigators at our clinical trial sites and our advisors to finalize the study protocol, making three rounds of minor changes to ensure that the protocol was clear and met all required human subjects requirements.
2. **Task 2:** Prepare sites for clinical trial
 - a. **Task 2a:** Conclude contractual agreements .We have concluded contractual agreements with four of the five trials sites. A fifth trial site, Tripler Army Medical Center, changed their contracting requirements, and asked us to complete an independent CRADA with them (their original plan had been for them to work through the Henry M Jackson

Foundation CRADA, which is supporting Walter Reed National Military Medical Center).

- b. **Task 2b:** Submit IRB materials. Our most important accomplishment was achieving HRPO clearance for our protocol, which occurred at the end of our year 1 activities. In addition, we (as the coordinating center) have received IRB clearance for the study. Three of our five sites (the VA sites) have received preliminary IRB clearance, and will rapidly receive final clearance pending very minor changes to protocol wording. Our two military medical center sites were required to wait to begin their IRB process until the HRPO clearance was final. They have now begun that submission process. Given this, we anticipate a staggered start to participant enrollment, with our VA sites beginning enrollment first and our military medical center sites beginning enrollment thereafter.
- c. **Task 2c:** Train site study staff on study procedures: We have reviewed the protocol extensively with the site Principal Investigators and relevant study staff. In addition, we have developed a complete training manual for study staff (covering the protocol and the supervision of the intervention and control cognitive training programs), and a complete assessment manual for cognitive raters (covering the administration, scoring, and data entry requirements for all of the inclusion/exclusion and assessment instruments in the study).
- d. **Task 2d:** Implement study database and electronic data collection system. We have completed the development of our electronic data capture system, programming all relevant fields for the consent, inclusion/exclusion, assessment, and adverse event data collection forms. We have also built the paper case report form binders, and integrated the paper (copyright) cognitive assessment materials into those binders to provide study staff with a complete record keeping system.

Key Research Accomplishments: Activities to date have been preparatory to the initiation of the multi-site clinical trial as planned. There have no research accomplishments during this preparatory period.

Reportable Outcomes: None to date

Conclusions: There are no research conclusions to date. We are eager to begin enrolling study participants in Q1 pending HRPO single site approval. Our study site principal investigators and study staff are highly motivated to start the trial.